REMARKS/ARGUMENTS

Claim Amendments

Claim 1 has been amended to recite "detecting and measuring gene copy number of a WIP1 gene in a breast tissue sample from the human that is suspected to be cancerous." This amendment is supported within the specification and does not introduce new matter.

Claim 60 has been cancelled.

Clams 1, 3, 54, 56-59 and 61-63 remain pending.

Specification and Drawing Amendments

Page 76 of the specification has been deleted and re-introduced as new Figure 6. Support for Figure 6 and the brief description of the new figure is found on deleted page 76 of the specification.

Objection to Specification

The submission filed April 24, 2002 is objected to because it allegedly introduces new matter into the disclosure. The Office Action asserts that SEQ ID NO:1 of the sequence listing is not identical to the sequence disclosed as SEQ ID NO:1 in the specification. Applicants respectfully point out that the nucleotide sequences are identical, however, the specification contains a nucleotide numbering difference when compared to the submission. The nucleotide numbering of SEQ ID NO:1 on original page 76 of the specification begins with the number 204, rather than 1. Applicants had

provided a corrected numbering of SEQ ID NO:1 in the submission, such that the numbering begins as it should at 1. In new Figure 6, which replaces original page 76, applicants also start the numbering of the sequence at 1. Thus, the now-correctly numbered SEQ ID NO:1 in the specification and SEQ ID NO:1 of the sequence listing are identical both in their numbering and as always was the case, in the actual nucleotide sequence. The corrected SEQ ID NO:1 is now found within Figure 6.

The disclosure is objected to because of an apparent page numbering problem. Page 76 was part of the original application as it was filed; it was submitted as the page following the Abstract (note that the Abstract bears page number 75). As best can be determined by applicant, on processing the original application, the USPTO moved the location of page 76 from following the Abstract to between pages 68 and 69 (*i.e.*, just prior to the claims). In any event, to expedite prosecution, page 76 now has been deleted from the specification and is being re-introduced as new Figure 6.

The disclosure is also objected to because it is allegedly unclear. The Office Action asserts that the nucleotide sequence at pages 36-37 and the nucleotide sequence at page 76 are not the same even though they are described as being GenBank entry NM_003620. Office Action at page 3, lines 20-21-page 4, lines 1-3. The specification does not indicate that the sequence on page 76 (now Figure 6) is identical to the sequence corresponding to GenBank accession number NM_003620, that was a supposition made by the Office Action. Rather, the GenBank accession number for WIP1 is NM_003620, and that is the sequence on pages 36-37. The coding sequence for WIP1, which is set forth on page 76, is not indicated as being identical to the sequence corresponding to GenBank accession number NM_003620. Nonetheless, since both nucleotides sequences

refer to or, are associated with the same WIP1 gene, *i.e.,* the gene which corresponds to GenBank entry NM_003620, that reference is noted in both locations. Applicants submit that in this context, the references do not confuse the skilled worker.

Claim Rejections under 35 U.S.C. §112, Second Paragraph

Claims 1, 3, 54, and 56-63 stand rejected under 35 U.S.C. §112 for being indefinite. Applicants respectfully traverse the rejection.

The Office Action asserts that it is "unclear how a WIP1 gene can 'comprise' or 'have' the indicated SEQ ID NOS, which are CDS and exclude introns, and still be a 'gene.'" Office Action at page 4, lines 18-19.

Claim 1 is amended to delete references to particular nucleotides. The claim as amended recites "detecting and measuring gene copy number of a WIP1 gene in a breast tissue sample from the human that is suspected to be cancerous." The nucleotide sequence for the WIP1 gene is well known in the art. An adequate written description of a gene which is well known in the art does not require a structural recitation either in the specification or in the claims. *See Capon v. Eshhar*, 418 F.3d 1349, 1360-61, 76 U.S.P.Q.2d 1078, 1087 (Fed. Cir. 2005). The claim as amended is definite.

Applicants respectfully request withdrawal of the rejection.

Claim Rejections under 35 U.S.C. §112, First Paragraph, Written Description

Claims 1, 3, 54, and 56-63 stand rejected under 35 U.S.C. §112 for failing to comply with the written description requirement. Applicants respectfully traverse the rejection.

The Office Action asserts that the version of SEQ ID NO:1, which was filed after the filing date, does not correspond to the sequence at page 76. Office Action at page 5, lines 8-9. The Office Action is mistaken. As explained earlier, these two sequences are the same – the only difference between the two sequences was the way in which the nucleotides were numbered. Applicants have amended the specification to correct the inadvertent nucleotide numbering difference that originally appeared on page 76. Thus, the submission of SEQ ID NO:1 is identical to the nucleotide sequence found on page 76, which is now Figure 6.

The Office Action also contends that the specification "does not teach that the sequence of the gene which was found to be amplified in Tables 1 and 2, or at pages 64 or 66, is SEQ ID NO:1 or SEQ ID NO:3." Office Action at page 6, lines 3-4. Applicants disagree with the Office Action's contention. The specification does support the sequence of the gene which was amplified in Tables 1 and 2. As discussed above, SEQ ID Nos 1 and 3 are sequences of the WIP1 gene. Further, the specification specifically teaches, "amplification and folds of overexpression were measured by Taqman and RT-Taqman respectively using WIP1 specific fluorogenic Taqman probes." Specification at page 41, lines 1 and 2, emphasis added. The specification also discloses that "[t]he nucleotide sequences of the WIP1 gene were used to design and make a suitable TaqMan probe set for WIP1." Specification at page 65, lines 23-24. The specification clearly states that the probes used for the Taqman polymerase chain reactions where specific for the WIP1 gene and thus supports the claims. The speculation voiced in the Office Action that the sequences could have some differences does not support the rejection in view of the clear indication in the specification to the contrary.

Further, the Office Action asserts that the specification "does not provide support for measuring gene copy number using RT-PCR." Office Action at page 6, lines 9-11. To advance prosecution claim 60 has been cancelled.

Applicants respectfully request withdrawal of the rejection.

Claim Rejections under 35 U.S.C. §112, First Paragraph, Enablement

Claims 1, 3, 54, and 56-63 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The Office Action asserts that it would require undue experimentation for one skilled in the art to perform the methods of the instant claims as written. Applicants respectfully traverse the rejection.

The Office Action asserts "the teachings of the specification do not address an association of the amplification of the WIP1 gene with *any* type of cancer...." Office Action at page 9, lines 11-13. The Office further asserts that, "[t]he specification does not teach or provide any working examples that WIP1 copy number is increased in precancerous lesions." Office Action at page 9, lines 18-19. Claim 1 is amended to delete references to precancerous lesions and lung tissue. The claim as amended recites "detecting and measuring gene copy number of a WIP1 gene in a breast tissue sample from the human that is suspected to be cancerous." Amended claim 1 does not associate amplification of the WIP1 gene with any type of cancer, or precancerous lesion; it specifically recites a breast cancer within a breast tissue.

The Office Action also contends that "the specification does not teach determining the sequence of the WIP1 gene that was amplified." Office Action at page 10, lines 8-9. In view of the clear teachings in the specification, to require that the

amplified gene be independently sequenced would have been unnecessarily redundant. As explained above, the specification does teach determining the sequence of the WIP1 gene. Both SEQ ID Nos. 1 and 3 contain sequences from the WIP1 gene. Further, the specification specifically teaches, "amplification and folds of overexpression were measured by Taqman and RT-Taqman respectively using WIP1 specific fluorogenic Taqman probes." Specification at page 41, lines 1 and 2, emphasis added. The specification clearly teaches that the sequence of the WIP1 gene, which is disclosed in the sequence listings and is well known in the art, is the amplified sequence present within the amplified region and thus fully enables the claims. Again, the Office Action's speculation concerning possible sequence differences does not provide support for the rejection.

Applicants respectfully request withdrawal of the rejection. No undue experimentation is required for one of skill in the art to perform the methods of the pending claims.

Claim Rejections under 35 U.S.C. §102

Claims 1, 2 (claim 2 was previously canceled), 54, 56, 57, 61, and 62 stand rejected under 35 U.S.C. §102 as being anticipated by Kallioniemi et al.[1], as defined by Wu et al.[2] and Genbank Accession number NM_003620. Applicants respectfully traverse the rejection.

To reject a claim as anticipated, each and every element as set forth in the claim must be found, either expressly or inherently described, in a single prior art reference.

[1] Kallioniemi *et al. Proc. Natl. Acad. Sci. USA,* vol. 91, pages 2156-2160, 1994.
[2] Wu *et al. Cancer Res.,* vol 61, pages 4951-4955, 2001.

Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631 (Fed. Cir. 1987). None of the cited references teaches each and every element recited in claims 1, 54, 56, 57, 61, and 62.

The Office Action states that "Wu teaches that the human WIP1 gene is located in the 17q22-23 region of chromosome 17. Kallioniemi teaches a method of detecting and measuring DNA sequence copy number increases for the 17q22-24 region in several human primary breast tumors and breast cancer cell lines." Office Action at page 14, lines 10-13.

A reference must provide a sufficient description of an invention and must provide guidance for selecting particular variables. *In re Ruschig*, 379 F.2d 990, 154 U.S.P.Q. 118 (C.C.P.A. 1967). Kallioniemi provides absolutely no guidance for associating amplification of any of the genes located within the 17q22-24 region with a breast cancer, let alone a disclosure associating amplification of WIP1 with a breast cancer. Further, Wu was published after the filing date of the subject application and does not qualify as prior art under 35 U.S.C. §102.

Kallioniemi does not teach each element recited in claim 1 and thus does not anticipate the claim. Reconsideration and withdrawal of the rejection over Kallioniemi and Wu is respectfully requested.

Claims 1, 2 (claim 2 was previously canceled), 54, 56, 57, 59, 61, and 62 stand rejected under 35 U.S.C. §102 as being anticipated by Orsetti et al.[3], as defined by Wu et al. and Genbank Accession number NM_003620. Applicants respectfully traverse the rejection.

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[3] Orsetti *et al.* Oncogene, vol 18, pages 6262-6270, 1999.

The Office Action asserts that Orsetti "teaches a method of detecting and measuring DNA sequence copy number increases over the entire 17q21-q24, including 17q21-qter, in 15 human breast tumors. . . ." Office Action at page 17, lines 10-12. The Office Action continues by stating that it "has sound basis for believing that some breast tumor samples which showed amplification of 17q22-q24 and 17q21-qter contained the gene which encoded the claimed sequences." Office Action at page 17, line 23 – page 18, lines 1-2.

Similar to the above rejection, the Office's rejection relies only on Orsetti's generic disclosure. Orsetti provides absolutely no guidance for associating amplification of any of the genes located within the 17q22-q24 and 17q21-qter regions with a breast cancer, let alone a disclosure associating amplification of WIP1 with a breast cancer. Reconsideration and withdrawal of the rejection over Orsetti and Wu is respectfully requested.

Claim Rejections under 35 U.S.C. §103

Claim 63 is rejected under 35 U.S.C. §103 as being unpatentable over Kallioniemi or Orsetti, each in view of Pinkel[4]. Applicants respectfully traverse the rejection.

The Office Action asserts that Kallioniemi teaches a method of detecting and measuring DNA sequence copy number increases for the 17q22-24 region in several cancer lines. Orsetti is cited as teaching a method of detecting and measuring DNA sequence copy number increases over the entire 17q21-q24 region. Pinkel is cited as teaching that arrays allow for high resolution analysis of DNA copy number using CGH. The Office Action further asserts that it would have been obvious to improve the method

[4] Pinkel *et al.* Nature Genetics, vol. 20, pages 207-211, 1998.

of Kallioniemi or Orsetti with the microarray based CGH method of Pinkel. Office Action at pages 18-19.

To reject a claim as *prima facie* obvious the Patent Office must meet three criteria:

> First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

MPEP § 2143. At a minimum, the Patent Office has failed to meet the third criterion.

As argued above, neither Kallioniemi nor Orsetti teach diagnosing a breast cancer by detecting gene copy number increases of WIP1. Thus, the references, even if combined, fail to teach or suggest all the claim limitations.

Applicants respectfully request withdrawal of the rejection.

Consideration and formal allowance of the pending claim are respectfully requested.

Respectfully submitted,

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Joseph M. Skerpon
Registration No. 29,864

BANNER & WITCOFF, LTD.
1001 G Street, N.W.
Washington, D.C. 20001
Telephone: (202) 824-3000

Amendments to the Drawings

The attached sheet of drawing is a new figure, Figure 6. New Figure 6 was an original part of the application as-filed, as original page 76.

Attachment – Figure 6